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PATENT
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This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

Claims 1 - 3 *(cancelled)*

4. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, comprising 1-5 targeting moieties.

5. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, comprising one targeting moiety.

Claims 6 - 11 *(cancelled)*

12. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, wherein **the linking group is of the formula:**

$((W^1)_h$-$(CR^{13}R^{14})_g)_x$-$(Z)_k$-$((CR^{13a}R^{14a})_{g'}$-$(W^2)_{h'})_{x'}$;

W^1 is $C(=O)NR^{15}$;

R^{15} is H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, C_1-C_5 alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

13. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47, wherein the linking group is of the formula:

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

14. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~10~~ **47**, wherein **the linking group is of the formula:**

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

W^1 is $C(=O)NR^{15}$;

R^{15} is H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, C_1-C_5 alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C_{1-5} alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

15. *(cancelled)*

16. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~10~~ **47**, wherein **the linking group is of the formula**:

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

x is 0;

k is 0;

R^{13a} and R^{14a} are independently H; or C_{1-5} alkyl substituted with 0-3 R^{16};

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with

0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

17. *(cancelled)*

18. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~10~~ **47**, wherein **the linking group is of the formula:**

$((W^1)_h-(CR^{13}R^{14})_g)_x-(Z)_k-((CR^{13a}R^{14a})_{g'}-(W^2)_{h'})_{x'}$;

W^1 is C=O;

h is 0, 1, or 2;

g is 2;

R^{13} and R^{14} are ~~independently~~ H;

x is 0, 1, 2, 3, 4, or 5;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

19. *(currently amended)* A ~~compound~~ **radiopharmaceutical** according to claim ~~10~~ **47**, wherein the linking group is absent.

Claims 20 - 46 *(cancelled)*

47. ***(currently amended)*** A radiopharmaceutical comprising a compound ~~of claim 1~~ and a cytotoxic radioisotope ~~which is complexed to the chelator;~~

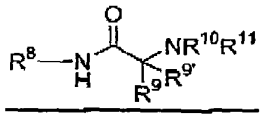
wherein said compound comprises:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <100 nM of the formula (Ib):



wherein,

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group, provided that when R^8 is phenyl, R^{10} is $-C(=O)-CHR^{12}-NH-CH(CH_3)-COOH$;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-2 additional heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted a bond to the linking group;

or alternatively,

R^9 and R^{10} are taken together with the nitrogen atom and carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-2 additional heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to the linking group; and

R^{12} is independently C_{1-20} alkyl.

Claims 48 - 49 ***(cancelled)***

50. ***(currently amended)*** A radiopharmaceutical **comprising:** ~~**according to claim 49 wherein the compound is**~~ **a cytotoxic radioisotope and a compound** selected from the group consisting of:

2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

wherein the cytotoxic radioisotope is ^{99m}Tc.

51. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of beta particle emitters, alpha particle emitters, and Auger electron emitters.

52. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, ^{212}Bi, ^{103}Pd, ^{109}Pd, ^{159}Gd, ^{140}La, ^{198}Au, ^{199}Au, ^{169}Yb, ^{175}Yb, ^{165}Dy, ^{166}Dy, ^{67}Cu, ^{105}Rh, ^{111}Ag, and ^{192}Ir.

53. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, ^{212}Bi, ^{103}Pd, and ^{105}Rh.

54. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, and ^{212}Bi.

55. ***(cancelled)***

56. ***(previously presented)*** A radiopharmaceutical composition comprising a radiopharmaceutical of claim 47, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

Claims 57 - 60 ***(cancelled)***

61. ***(currently amended)*** A radiopharmaceutical kit comprising a radiopharmaceutical of ~~Claim 47~~ **claim 47**, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

62. ***(currently amended)*** A **radiopharmaceutical** kit of ~~Claim 60~~ **claim 61** further comprising a stabilizer.

63. ***(currently amended)*** A radiopharmaceutical kit according to ~~Claim 60~~ **claim 61**, wherein the radioisotope is ^{186}Re or ^{188}Re and the kit further comprises one or more ancillary ligands and a reducing agent.

64. ***(currently amended)*** A radiopharmaceutical kit according to ~~Claim 63~~ **claim 63**, wherein the ancillary ligands are tricine and a phosphine.

Claims 65 - 67 *(cancelled)*

68. *(currently amended)* A method of treating a pathological disorder mediated by a matrix metalloproteinase in a patient which comprises ~~administring~~ administering to a patient in need thereof a therapeutically effective amount of a radiopharmaceutical according to claim 47 and a pharmaceutically acceptable carrier.

Claims 69 - 71 *(cancelled)*

72. *(original)* A method of inhibiting proliferation of cancer cells, comprising contacting the cancer cells with a proliferation-inhibitory amount of a radiopharmaceutical of claim 47.

73. *(previously presented)* A method of claim 68, wherein the matrix metalloproteinase is selected from the group consisting of: MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

74. *(previously presented)* A method of claim 68 wherein the matrix metalloproteinase is selected from the group consisting of: MMP-2, MMP-9, and MMP-14.

Claims 75 - 77 *(cancelled)*

78. *(currently amended)* A process for the preparation of a radiopharmaceutical, said process comprising generating a macrostructure from a plurality of molecular components wherein the plurality of components ~~includes a compound of claim 1 and a cytotoxic radioisotope~~ comprises a radiopharmaceutical according to claim 47.

79. *(cancelled)*